Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

dimethomorph (ISO); (*E*,*Z*)-4-(3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)acryloyl)morpholine

EC Number: 404-200-2
CAS Number: 110488-70-5; (1135441-72-3)

CLH-O-0000001412-86-298/F

Adopted

20 September 2019

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON DIMETHOMORPH (ISO); (E,Z)-4-(3-(4-CHLOROPHENYL)-3-(3,4-DIMETHOXYPHENYL)ACRYLOYL)MORPHOLINE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the public consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the public consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties.

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Substance name: dimethomorph (ISO); (E,Z)-4-(3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)acryloyl)morpholine
EC number: 404-200-2
CAS number: 110488-70-5
Dossier submitter: The Netherlands

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
07.03.2019	Denmark		MemberState	3
Comment received				
We propose to make it clear that the CLH proposal was only open for reproductive toxicity on human health. Hence, other endpoint such as STOT RE has not been taken into consideration. This is important as often the harmonized classification after renewals of pesticides are considered to cover all toxicological endpoints.				
Dossier Submitter's Response				
As presented in table 7 of the CLH report, reproductive toxicity is the only human health endpoint within the scope of the public consultation. As indicated in section 10.10 (specific target organ toxicity – repeated exposure) of the CLH-report, data on repeated dose toxicity are provided only in support of the assessment of the human health endpoint reproductive toxicity.				
RAC's response				
Reproductive toxicity is the only human health endpoint evaluated by RAC. The data from repeated dose toxicity are considered as supportive evidence of reproductive toxicity.				

Date	Country	Organisation	Type of Organisation	Comment number
07.03.2019	Germany		MemberState	4
Comment received				
We agree that the endpoints reproduction and development are of most concern for this substance and should be considered in detail. However, the prostate findings as observed in short-term studies in dogs (see below) might also trigger classification for STOT-RE 2 if not used to support the prosed classification for reproductive toxicity. This approach has been also discussed in the re-evaluation of dimethomorph under Regulation (EC) 1107/2009. In fact, STOT-RE 2 has been proposed by the RMS (i.e., the Netherlands) and				

was supported by the Co-RMS (Germany) and, very recently, by MS experts. Therefore, we would like to suggest to the RAC that also this endpoint is taken into consideration even though it was not specifically assessed by the DS.

The used CAS and EC numbers are for the E/Z isomer. There is also a list number available for the single Z-isomer. In case this "pure" isomer should also be covered by the CLH proposal this needs to be clearly stated in chapter 1 of the report and also on the front page of the report. Otherwise the classification will apply only to the isomeric mixture.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comment by the DE-CA on the CLH proposal for dimethomorph as Repr. 1B.pdf

Dossier Submitter's Response

- Current CLH-dossier focusses, with respect to human health, only on the endpoint reproductive toxicity. We take note of your suggestion to RAC to include the endpoint STOT-RE in their evaluation as well.
  See our response to comment number 7 with respect to the relevance of the prostate findings for the endpoint reproductive toxicity.
- This CLH-proposal focusses on Dimethomorph (ISO); (E,Z)-4-(3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)acryloyl)morpholine with CAS 110488-70-5 and EC 404-200-2. This chemical is authorized as an active substance within the context of Regulation (EC) 1107/2009 and currently included in Annex VI of the CLP-regulation with index-number 613-102-00-0.

RAC's response

STOT RE is not a subject to evaluation in this dossier. Findings from the repeated dose studies (including effects on prostate) are considered for the endpoint reproductive toxicity.

Date	Country	Organisation	Type of Organisation	Comment number
05.03.2019	France		MemberState	5

Comment received

FR:
- p.1: Identity of the substance, Table 1: Unit (g/mol) of the molecular weight should be added.

- p.4: Table 7: For the following hazard classes – explosives, flammable solids, oxidizing solids – it should be better to indicate in the column reason for no classification, "data conclusive but not sufficient for classification" rather than "hazard class not assessed in this dossier" as data are available in RAR of the substance

- p.5-6: Physicochemical properties, Table 8: purity of the test substance could be added for each property.

- p.6: For flash point and viscosity, it should be better to add "non relevant as the substance is solid".

- p.6: For the following properties – self-ignition temperature, granulometry and stability in organic solvents – it should be better to add "no data".

- p.6-7: Evaluation of physical hazards: for explosives, flammable solids and oxidising solids points: data are available in the RAR of the substance (the used method, the results and the reference of the studies), this should be added in the CLH report.
Dossier Submitter's Response
The comments are noted. Unfortunately, the CLH-report including its tables 7 and 8 cannot be updated at this stage of the CLH-process. Moreover, current CLH-dossier focusses on two endpoints, i.e. reproductive toxicity and hazardous to the aquatic environment, as indicated in table 7. An evaluation of the physical hazards (i.e. chapter 8 of the CLH-report) has therefore not been included.
RAC's response
Thank you for the comment, please note the physical hazards were not part of the CLH proposal and thus not evaluated by RAC.

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
28.02.2019	Denmark	DTU Food	Academic institution	6
Comment received				
Reproductive toxicity and Endocrine disruption. The report (see references below) concludes: Deltamethrin does not meet the WHO definition of an endocrine disruptor, but fulfil the WHO definition of a potential endocrine disruptor. Also deltamethrin fulfil the proposed Danish criteria for being a suspected ED. Hass, U., Christiansen, S., Andersen MD, Rosenberg SA, Egebjerg KM, Brandt S, Nikolov NG, Holbech H, Morthorst JE (2018) List of Endocrine Disrupting Chemicals. Report from Danish Centre on Endocrine Disrupters for Danish EPA link to report: http://cend.dk/files/DK_ED-list-final_2018.pdf, link to appendix http://cend.dk/files/DK_ED-list-final_appendix1_2018.pdf I have uploaded deltamethrin information and litterature only (page 1-20) ECHA note – An attachment was submitted with the comment above. Refer to public attachment DK_ED list final_appendix Deltamethrin_2018.pdf				
Dossier Submitter's Response				
The comments are noted. The Dossier Submitter would like to point out that current CLH-dossier focusses on the chemical Dimethomorph and not on Deltametrin.				
RAC's response				
RAC agrees with DS that subject of the current CLH proposal is dimethomorph and not deltametrin.				

Date	Country	Organisation	Type of Organisation	Comment number
08.03.2019	Spain		MemberState	7
Comment received				
Fertility In the dog 90-day and 1-year study increased prostate weight combined with prostatic interstitial fibrosis was observed. These effects were observed in presence of other general toxicity. Besides, no such effects were observed in the repeated dose studies with rats and mice. These effects doesn´t seem as sufficiently convincing to warrant classification for fertility.				

In the reproductive toxicity studies no effect on the mating index, fertility index, gestation index, live birth index and sperm parameters was observed.

In the extended one generation study, there were significant variations of the relative weight of some reproductive organs in both F1 cohorts, as decrease of the seminal vesicle and reduction in the prostrate relative weight. However, they were not accompanied by effects in gross necropsy or histopathology. Due to lack of correlates between weight changes and morphology, findings observed are not specific hallmarks for adverse effects on reproductive functions.

There is evidence for a statistically significantly reduced gestation length in the extended one generation study. The reduced gestation length was observed in the presence of maternal toxicity. We consider this marginal reduction in gestation length of low concern in absence of alteration in mating/ sexual behavior.

Effects observed are due to in utero exposure and are supportive of developmental toxicity and that no classification is required for dimethomorp for effects on sexual function and fertility.

On overall, the Spanish CA concludes that there is no clear evidence for an adverse effect on sexual function or fertility. No classification for effects on fertility is warranted.

Development

In the extended one-generation a decreased anogenital length and a delay in preputial separation was observed in males (F1) at the 800 ppm and 1600 ppm (both effects were outside of the historical control range). A decrease in absolute and relative seminal vesicle and prostate weight was observed in the adult F1 at 800 and 1600 ppm without histopathological changes. Besides, at 1600 ppm, mean pup body weight was 13% below control at PND 1 and still 9% below controls at PND 21. Parental toxicity was evident from the dose of 800 ppm (decreased body weight gain in males F0, liver toxicity).

The statistical significance decrease of anogenital distance (AG) in F1 pups at 800 ppm was unclear as the AG index at 800 ppm was within the range of historical controls. Only the statistical significance decrease of AG in F1 males at the high dose of 1600 ppm is considered treatment related. However, this was a very weak effect, as the anogenital index of 1.57 at 1600 ppm in F1 males was only slightly below historical controls (1.58-1.67). Besides, the statistical significance of these reductions in the anogenital distance at 800 and 1600 ppm can be influenced by the high value of the anogenital distance in controls (3.15) since it represents the highest value in the provided historical control range (2.99-3.15). In addition, this effect was not associated with changes in sex ratio/ or sexual development.

The delay in preputial separation (PPS) at the mid dose of 800 ppm was shown to be

caused by the decreased body weight of the offspring. For the high dose group a specific effect on PPS could not be excluded. The delay in preputial separation at 1600 ppm is considered to be only a developmental effect as there was no impairment of the sexual function in the two reproduction toxicity studies.

The Spanish CA is of the opinion that findings observed in the extended one-generation study (reduced anogenital distance, delay in preputial separation, reduced pup weight and reduced seminal vesicle and prostate weight) are indicative of effects on development. Based on the in vitro information a non-maternally mediated mode of action through the anti-androgenic properties of dimethomorph seems likely. The observed effects are therefore considered to be related to the anti-androgenic effect of dimethomorph and not secondary to maternal toxicity. This mode of action is considered to be relevant to humans and therefore classification for developmental toxicity is considered necessary. However, the whole available data indicate that severity of the effects is not sufficiently convincing to classified dimethomorph as Repr 1B for effects on development as proposed by the dossier submitter. The Spanish CA considers that the overall available evidence is deemed to best match the criteria for classification as category 2 for developmental effects.

Dossier Submitter's Response

We take note of your comments concerning adverse effects on fertility and sexual function. The Dossier Submitter considers the effects on prostate as adverse and relevant for classification. In the 90-day and 1-year dog studies *decreased** prostate weight combined with prostatic interstitial fibrosis was observed. Although it is noted that these effects were observed in presence of general toxicity, it cannot be excluded that these are primary effects on the reproductive system. Given this uncertainty, it was considered that these would justify a category 2 classification for reproductive toxicity. This is further substantiated as such effects were only observed in dog and not in mouse or rat.
The Dossier Submitter considers the statistically significant reduction in gestation length as observed in the extended one-generation reproductive toxicity study as adverse and relevant for humans, and therefore considers this as a clear evidence for an adverse effect on fertility or sexual function, which would justify the cat. 1B proposal.

With respect to the adverse effects on development, the Dossier Submitter considers the reduced anogenital distance and the delayed puberty/sexual maturation as noticed in the extended one-generation reproductive toxicity study as adverse effects which are relevant for humans and conclude that there is clear evidence for an adverse effect on development.

* see our response to comment nr 10; The summarized findings on page 13 (sections 10.8.2 and 10.8.3) of the CLH-report contain an error; it should state "In the dog 90-day and 1-year study **decreased** prostate weight combined with prostatic interstitial fibrosis was observed."

RAC's response

Under CLP (Annex I: 3.7.1.3), it is recognised that adverse effects on sexual function and fertility include effects on the onset of puberty. Thus RAC considers the delayed sexual maturation in males observed in the extended one-generation reproduction toxicity study as clearly adverse and relevant for classification on sexual function and fertility. A decrease in absolute and relative seminal vesicle and prostate weight reported in the same study are in line with the proposed anti-androgenic mode of action and support the classification for sexual function and fertility. Further evidence is provided from repeated dose studies in dogs where prostate weight is significantly reduced by up to 62%. With

respect to developmental toxicity, severity of the effects from the EOGRTS (i.e., decreased pup weight) is not sufficient for classification. The effect on anogenital distance is a marker reflecting in utero anti-androgenicity and it is an effect on development, but as such not sufficient for classification.

Date	Country	Organisation	Type of Organisation	Comment number
07.03.2019	Denmark		MemberState	8

Comment received

Repro 1B:
DK agrees with the proposed classification Repr 1B (H360FD) for the following reasons:

Development
Based on decreased anogenital distance, delayed sexual maturation observed as delayed preputial separation in males and delayed vaginal opening in females, decrease seminal vesicle, decrease prostate weight, and decreased pup weight observed in the extended one-generation classification on development is warranted. Maternal toxicity was not so severe and cannot explain the developmental findings. The effects are relevant for humans. Hence, classification as Repr. 1B; H360D is warranted.

Sexual function and fertility
Based on reduced gestation length observed in the extended one generation toxicity study a classification on sexual function and fertility is warranted. This effect was also indicated in the older 2-generation study.
The effects on prostate (90-day and 1-yr dog studies and extended one generation study) and testes (hyperplasia in 2-yr rat and increased weight 1-yr dog) also indicate potential damage of the male fertility and could be taken into consideration for classification.
Effects on parturition (reduced gestation length) relevant for humans was observed in addition to alterations of the male reproductive system. Hence, classification as Repr. 1B; H360F is warranted.

STOT RE 2:
Classification as STOT-RE 2 should be considered based on the prostate findings such as histopathology (interstitial fibrosis) and decrease prostate weight in both the 90 day and 1 year dog studies. The effects were observed at 43 and 47 mg/kg bw/d and were reproducible within the species and with different dossing pattern (90 day vs 1 year). In addition, reduced prostate weight was observed in the extended one generation study in rats.
The prostate is a target organ of dimethomorph. However, the effects on prostate could perhaps also be considered for the classification on fertility.

Dossier Submitter's Response

Thank you for your support.
See our response to comment number 7 with respect to the relevance of the prostate findings for the endpoint reproductive toxicity.

RAC's response

The delayed sexual maturation and decreases in seminal vesicle and prostate weights are considered by RAC as adverse effects on sexual function and fertility. With respect to developmental toxicity, severity of effects (i.e., decreased pup weight) appears not sufficient for classification. The effect on anogenital distance is a marker reflecting in utero anti-androgenicity and it is an effect on development, but as such not sufficient for classification. STOT RE classification is not under the scope of this CLH proposal.

Date	Country	Organisation	Type of Organisation	Comment number
07.03.2019	France	BASF	Company-Manufacturer	9
Comment received				
1/ BASF strongly disagrees with the dossier submitters proposal for Repr. 1B H360FD. The classification for fertility and development is clearly disproportionate in relation with the observed effects. See details in the attached documents "Commenting table" and Doc 2017/1033551. 2/ STOT RE2 is not proposed in the CLH report and BASF fully agree with that. (CLH report 10.10.1 p 28). See details in the document "Commenting table" 3/ Following the new EFSA/ECHA Guidance document for identification of ED, a full Assessment is provided to EFSA, which should be added for completeness. (Annex I 3.10.3). See details in the attached documents "Commenting table and Doc 2018/1202679. ECHA note – An attachment was submitted with the comment above. Refer to public attachment Documents to ECHA.zipx				
Dossier Submitter's Response				
The comments are noted. Unfortunately, the CLH-report cannot be updated at this stage of the CLH-process. Thank you for providing us the results of the ED assessment. We take note of your comments concerning our conclusion with respect to adverse effects on fertility and sexual function. However, the Dossier Submitter considers the statistically significant reduction in gestation length as observed in the extended one-generation reproductive toxicity study as adverse and relevant for humans, and therefore considers this as a clear evidence for an adverse effect on fertility or sexual function. With respect to the adverse effects on development, the Dossier Submitter considers the reduced anogenital distance and the delayed sexual maturation as noticed in the extended one-generation reproductive toxicity study as adverse effects which are relevant for humans. These effects are considered not to be a secondary non-specific consequence of the observed maternal toxicity. Therefore we conclude that there is clear evidence for an adverse effect on development. See our response to comment number 7 with respect to the relevance of the prostate findings for the endpoint reproductive toxicity.				
RAC's response				
Thank you for the detailed analysis of the reproductive toxicity of dimethomorph. The results from the EOGRTS in the rat in combination with data from repeated dose studies in dogs are considered to provide clear evidence for an adverse effect on sexual function and fertility.				

Date	Country	Organisation	Type of Organisation	Comment number
07.03.2019	Germany		MemberState	10
Comment received				
see attached comment ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comment by the DE-CA on the CLH proposal for dimethomorph as Repr. 1B.pdf				

Dossier Submitter's Response

Thank you for your comments.

a) adverse effects on sexual function and fertility
In the table below, an overview is presented on the individual animal data on gestational length in the extended one-generation reproductive toxicity study (2014a). This overview indicates that there are no true outliers with respect to reduced gestation length.

Overview of individual data on gestation length in the extended one-generation rat reproductive toxicity study (2014a)

control		**low**		**mid**		**High**	
Animal no	*Gestation length (d)*	*Animal no*	*Gestation length (d)*	*Animal no*	*Gestation length (d)*	*Animal no*	*Gestation length (d)*
101	*	126	22	151	22	176	22
102	22	127	22	152	22	177	21
103	23	128	23	153	22	178	21
104	22	129	22	154	22	179	21
105	22	130	22	155	22	180	21
106	22	131	22	156	22	181	21
107	22	132	22	157	22	182	**
108	23	133	**	158	22	183	21
109	22	134	23	159	22	184	22
110	23	135	22	160	22	185	22
111	22	136	22	161	23	186	21
112	23	137	22	162	21	187	21
113	22	138	22	163	23	188	22
114	23	139	22	164	22	189	21
115	22	140	22	165	22	190	21
116	22	141	22	166	22	191	22
117	23	142	23	167	22	192	21
118	23	143	22	168	21	193	22
119	23	144	23	169	23	194	22
120	22	145	22	170	22	195	22
121	22	146	**	171	22	196	**
122	22	147	22	172	22	197	**
123	22	148	22	173	22	198	21
124	22	149	22	174	22	199	22
125	22	150	22	175	22	200	21
mean	*22.3*	*mean*	*22.2*	*mean*	*22.0*	*mean*	*21.4*

* sacrificed premature
** pregnant status: GD0; implants; no pups

The Dossier Submitter considers the statistically significant reduction in gestation length as observed in the extended one-generation reproductive toxicity study as adverse and relevant for humans, and therefore considers this as a clear evidence for an adverse effect on fertility or sexual function.

With respect to the reduced anogenital distance and the delayed puberty/sexual maturation as noticed in the extended one-generation reproductive toxicity study, these are considered as adverse effects which are relevant for humans. The Dossier Submitter therefore considers that these should be taken forward for classification for adverse effect on reproductive toxicity and a cat. 1B classification would be justified in our opinion. The

Dossier Submitter agrees that it can be questioned whether this is an effect on fertility or development and would correspond to an H361f or H361d. In contrast to the DSD-criteria, the current criteria do not provide a strict distinction for these kind of effects: adverse effects on sexual function and fertility include "*adverse effects on onset of puberty*" and adverse effects on development of the offspring includes "*any effect… resulting from … exposure of the developing offspring during prenatal development, or postnatally, to the time of sexual maturation*". The Dossier Submitter considered these as an adverse effect on development.

With respect to the effects on prostate, thank you for your detailed evaluation. The Dossier Submitter agrees that prostate can be considered a target organ. We further agree that these effects can be considered as adverse and relevant for classification. It is noted that the summarized findings on page 13 (sections 10.8.2 and 10.8.3) of the CLH-report contain indeed an error; it should state "In the dog 90-day and 1-year study **decreased** prostate weight combined with prostatic interstitial fibrosis was observed." See further our response to comment number 7 with respect to the relevance of the prostate findings for the endpoint reproductive toxicity.

b) adverse effects on development of the offspring
See above for our response to the comments concerning the reduced anogenital distance and the delayed puberty/sexual maturation.

RAC's response

Thank you for providing individual data on gestation length from the EOGRTS. RAC considers the delayed onset of puberty in males as a clearly adverse effect relevant for classification on sexual function and fertility. Effects on prostate (decreased weight and fibrosis) are considered as supportive evidence for sexual function and fertility impairment. With respect to developmental toxicity, severity of the remaining effects appears not sufficient for classification. The effect on anogenital distance is a marker reflecting in utero anti-androgenicity and it is an effect on development, but as such not sufficient for classification.

Date	Country	Organisation	Type of Organisation	Comment number
05.03.2019	France		MemberState	11

Comment received

FR:
- 10.8.3 Comparison with the CLP criteria (fertility)
The proposal for classification repr. cat1B H360F is supported based on effects observed in the EOGRT in line with anti-androgenic properties of Dimethomorph:
* Decreased gestation length (also observed in the two generation reproductive study)
* Decreased anogenital distance
* Delay in preputial separation
Furthermore, prostate effects (decreased weight and fibrosis) observed in dogs also support potential impact on male fertility.

- 10.8.3 Comparison with the CLP criteria (development)
Effects such as decreased anogenital distance, delay in preputial separation and decreased absolute and relative seminal vesicle and prostate weight cannot be clearly assigned to either impairment of sexual function and fertility or to developmental toxicity.

However, since those effects are induced during pregnancy, and/or result from parental exposure, classification repr.cat1B H360D seems also warranted.
Dossier Submitter's Response
Thank you for your support. See our response to comment number 7 with respect to the relevance of the prostate findings for the endpoint reproductive toxicity.
RAC's response
Delayed sexual maturation and prostate effects (decreased weight and fibrosis) are in line with the proposed anti-androgenic properties of dimethomorph and considered adverse to fertility and sexual function. With respect to developmental toxicity, severity of the remaining effects appears not sufficient for classification. The effect on anogenital distance is a marker reflecting in utero anti-androgenicity and it is an effect on development, but as such not sufficient for classification.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
08.03.2019	United Kingdom		MemberState	12

Comment received

Dimethomorph EC: 404-200-2; CAS: 110488-70-5)
We agree the data support chronic classification endpoints in the range 0.1 to 1 mg/l resulting in Aquatic Chronic 2.

We are unclear if the P. Promelas 34-d NOEC of 0.107 mg/l (mm) based on embryo hatching is a true NOEC as a clear dose-response effect was not observed due to effects only at one treatment and none at the treatment above which was highest treatment. For example has the data been tested for an outlier? It might be useful to consider if similar mortality was observed in across the replicates for the 0.33 mg a.s./l (nominal) treatment.

We note that test concentrations have been measured in the chronic toxicity study with A. bahia - while the NOEC has been based on mean measured concentrations, the EC10 reproduction is based on nominal concentrations. As measured concentrations are not within 20% of the nominal, for completeness it would be useful to present the EC10 based mean measured concentrations.

Dossier Submitter's Response

Thank you for your support.
Where it concerns the P. promelas study, results for hatching in separate replicates is givenin the following table:

Nominal concentration	**Mean measured concentration**	**day0**	**hatched larvae**	
mg/L	**mg/L**	**Number**	**Number**	**hatched**
0	0	25	21	84
(Control)		25	21	84
		25	21	84
		25	22	88
0.01	0.0082	25	20	80

		25	20	80
		25	20	80
		25	20	80
0.033	0.0310	25	23	92
		25	23	92
		25	21	84
		25	20	80
0.1	0.107	25	19	76
		25	21	84
		25	20	80
		25	21	84
0.33	0.347	25	17	68
		25	17	68
		25	19	76
		25	18	72
1	0.92	25	18	72
		25	19	76
		25	19	76
		25	19	76

From this it can be concluded that results within one test concentration are rather similar. It should also be noted that, although not significant, a reduction was also observed in the highest test concentration.

For the A. bahia study, an EC10 calculated on mean measured values is not available. Although individual measured concentrations are at some points slightly over 20% of nominal, the mean measured concentrations are within 20% of nominal as can be seen in the tabel below.

Concentration [mg a.s./L] (nominal)	Control	0.065	0.13	0.25	0.50	1.0
Concentration [mg a.s./L] (mean measured)	--	0.0582	0.119	0.241	0.502	0.997

RAC's response

Thank you for your comment. RAC notes the support for the proposed environmental classification as Aquatic Chronic 2 based on endpoints in the range 0.1 to 1 mg/L.

RAC would like to thank the DS for additional data for chronic toxicity study with *P. promelas*. RAC notes that the results within one test concentration are rather similar and that not significant reduction was observed in the highest test concentration.

RAC appreciates the clarification provided by the DS regarding the toxicity values in chronic toxicity study with invertebrate *A. bahia*.

During the public consultation, a Company-Manufacturer (see comment 13) pointed out that reliable EC_{50} and NOEC values based on mean measured concentrations for algae *P. subcapitata* are available. RAC considered this additional data in the opinion development. The new provided values (72-h E_rC_{50} of 65.6 mg/L and 72-h $NOEC_r$ of 5.4 mg/L) are higher than the key values (96-h EC_{50} = 4.42 mg/L for *C. virginica* and 34-d NOEC = 0.107 mg/L for fish *P. promelas*) used for classification of the substance for acute and chronic hazard. Therefore, on the basis of the available data, RAC considers that dimethomorph should be

classified as Aquatic Chronic 2 based on 34-d NOEC of 0.107 mg/L for fish *P. promelas* and lack of rapid degaradbility. This is consistent with the conclusion of the DS.

Date	Country	Organisation	Type of Organisation	Comment number
07.03.2019	France	BASF	Company-Manufacturer	13

Comment received

The CLH report states that the algal study by Jatzek is not reliable because actual mean measured concentrations were not presented in the RAR and a NOEC cannot be determined. This study is considerable acceptable by the RMS in the revised RAR, so please consider the additional information.
(CLH report 11.6.3 p42) See additional information in the attached document "Commenting table"

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Documents to ECHA.zipx

Dossier Submitter's Response

In the latest version of the RAR, mean measured concentrations are now reported and EC50 and NOEC values are re-calculated for growth rate and yield based on geometric mean measured concentrations (ErC50 = 65.6 mg/L, NOECr = 5.4 mg/L; EyC50 = 26.5 mg/L, NOECy = 5.4 mg/L). With the new information available these endpoint can be considered suitable for classification purposes. As these values are higher than the key values used for the current classification proposal, these will not affect the current proposal.

RAC's response

Thank you for your comment. RAC notes that in the latest version of the RAR from January 2019, EC_{50} and NOEC values based on mean measured concentrations are reported for acute toxicity study carried out on algae *Pseudokirchneriella subcapitata* (Jatzek, 2001). Furthermore, RAC notes that the study meets all validity criteria according to current version of OECD TG 201 and it is considered acceptable by the RMS and DS. RAC is of the opinion that it is appropriate to consider this data relevant for classification of the substance.

According to current CLP Guidance (Version 5.0, July 2017), the endpoint based on growth rate reduction is preferred for algae. Therefore the 72-h E_rC_{50} of 65.6 mg/L and 72-h $NOEC_r$ of 5.4 mg/L were selected as the lowest values for this species by RAC. RAC shares the view with the DS that the new provided values are higher than the key value (34-d NOEC = 0.107 mg/L for fish *P. promelas*) used in the current classification proposal and do not affect proposed acute and chronic classification. RAC considers that dimethomorph should be classified as Aquatic Chronic 2 based on 34-d NOEC of 0.107 mg/L for fish *P. promelas* and lack of rapid degaradbility. This is consistent with the conclusion of the DS.

Date	Country	Organisation	Type of Organisation	Comment number
07.03.2019	Germany		MemberState	14

Comment received

We support the proposal for classification as Aquatic chronic 2 (H411).

Dossier Submitter's Response

Thank you for your support.

RAC's response
Thank you for your comment. RAC notes the support for the proposed environmental classification. During the public consultation, a Company-Manufacturer (see comment 13) pointed out that reliable EC_{50} and NOEC values based on mean measured concentrations for algae *P. subcapitata* are available. RAC considered this additional data in the opinion development. The new provided values (72-h E_rC_{50} of 65.6 mg/L and 72-h $NOEC_r$ of 5.4 mg/L) are higher than the key values (96-h EC_{50} = 4.42 mg/L for *C. virginica* and 34-d NOEC = 0.107 mg/L for fish *P. promelas*) used for classification of the substance for acute and chronic hazard. Therefore, on the basis of the available data, RAC considers that dimethomorph should be classified as Aquatic Chronic 2 based on 34-d NOEC of 0.107 mg/L for fish *P. promelas* and lack of rapid degaradbility. This is consistent with the conclusion of the DS.

Date	Country	Organisation	Type of Organisation	Comment number
05.03.2019	France		MemberState	15
Comment received				
FR: We agree with the proposal of classification for environmental hazards.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you for your comment. RAC notes the support for the proposed environmental classification. During the public consultation, a Company-Manufacturer (see comment 13) pointed out that reliable EC_{50} and NOEC values based on mean measured concentrations for algae *P. subcapitata* are available. RAC considered the additional data in the opinion development. The new provided values (72-h E_rC_{50} of 65.6 mg/L and 72-h $NOEC_r$ of 5.4 mg/L) are higher than the key values (96-h EC_{50} = 4.42 mg/L for *C. virginica* and 34-d NOEC = 0.107 mg/L for fish *P. promelas*) used for classification of the substance for acute and chronic hazard. Therefore, on the basis of the available data, RAC considers that dimethomorph should be classified as Aquatic Chronic 2 based on 34-d NOEC of 0.107 mg/L for fish *P. promelas* and lack of rapid degaradbility. This is consistent with the conclusion of the DS.				

PUBLIC ATTACHMENTS
1. Documents to ECHA.zipx [Please refer to comment No. 9, 13]
2. Comment by the DE-CA on the CLH proposal for dimethomorph as Repr. 1B.pdf [Please refer to comment No. 4, 10, 14]